

**OPTN/UNOS *Ad Hoc* Disease Transmission Advisory Committee**  
**Report to the Board of Directors**  
**June 21-22, 2010**  
**Richmond, Virginia**

**Summary**

**I. Action Items for Board Consideration**

- None

**II. Other Significant Items**

- The Committee reviewed feedback received thus far on its proposed modifications to Policies 2.0 and 4.0, which are currently out for public comment. (Item 1, Page 3)
- The Committee received an update from its Living Donor Screening Subcommittee regarding its proposed suggestions to the Living Donor Committee on infectious disease and cancer screening for potential living donors. (Item 3, Page 4)
- The Committee completed its semi-annual review and classification of potential disease transmission events reported to the Patient Safety System. (Item 4, Page 7)
- The Committee received an update on the Malignancy Subcommittee's draft manuscript that offers categorizations for donor tumor risk transmission and reviewed malignancy data requested during the September 2009 meeting. (Item 5, Page 7)
- The Committee received an update from the Newsletter Subcommittee regarding the number of readers for its February 2010 first edition and discussed plans for an upcoming issue. (Item 7, Page 17)
- The Committee reviewed and discussed a proposal to clarify and improve policies on importing foreign deceased donor organs under development by the Ad Hoc International Relations Committee. (Item 9, Page 17)
- The Committee discussed the development of a follow-up OPO survey regarding donor screening practices. (Item 11, Page 20)

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**Michael G. Ison, MD, MS, Chair**  
**Michael Nalesnik, MD, Vice Chair**

*This report reflects the work of the Ad Hoc Disease Transmission Advisory Committee (DTAC) during its April 14, 2010, meeting in Chicago, Illinois, as well as all monthly case review conference calls. Additionally, the Committee's Living Donor Screening and Policy Rewrite Subcommittees have met by teleconference and LiveMeeting<sup>®</sup> since the DTAC reported to the Board in November, 2009.*

1. Current Proposal Feedback Review

The Committee developed a proposal to modify Policies 2.0 (Minimum Procurement Standards for An Organ Procurement Organization), 4.0 (Acquired Immune Deficiency Syndrome (AIDS), Human Pituitary Derived Growth Hormone (HPDGH), and Reporting of Potential Diseases or Medical Conditions, Including Malignancies, of Donor Origin) and 5.5 (Documentation Accompanying the Organ or Vessel), which was released for public comment on March 19, 2010. It reviewed feedback received thus far during its April 14, 2010, meeting. To date, three committees had reviewed and supported the proposal, and Region 10 voted against it as written.

Pancreas Transplantation Committee: The Committee considered this proposal on March 26, 2010. Committee members noted there could be confusion about the differences in method in how a specimen is qualified. OPO representatives noted that it would not be a burden for the OPO to tell the transplant centers whether the sample was hemodiluted. It would be a burden if the OPO were required to retrieve a new sample and re-test if the original sample were hemodiluted. The Committee voted to support the proposal as written. (9-Support, 0-Oppose, 0-Abstain)

*The Committee appreciates this feedback. Reporting the use of a hemodiluted specimen for serologic testing is not expected to be burdensome, and the Committee does not have plans to pursue requiring the retrieval of a new, qualified sample for testing when hemodilution occurs.*

Only one region had convened at the time of this meeting. Region 10 did not vote in support of the proposal. Formal response was not yet available from Regional Administration, but the presenter shared feedback regarding toxoplasma screening for potential heart donors, patient safety contact, serum storage, and hemodilution. It was noted that Region 10 felt that the proposals placed a heavy burden on the OPOs and the transplant centers without any comment on who would financially support the reporting service 24/7. Also, the issue of where to record this information was raised. DonorNet<sup>®</sup> may not be appropriate for added or modified information because it does not track when changes were made, and this creates challenges for both the OPO and transplant center. The Committee will respond formally to Region 10's concerns once it receives written feedback at the end of the public comment period.

Because the public comment period does not end until July 16, 2010, the Committee will reconvene via teleconference to review any additional responses that were not available for consideration at the time of this meeting.

The Chair indicated that in the future he would prefer a more formal process in developing such proposals as a joint effort with joint sponsorship. A joint subcommittee was formed with representation from both the OPO and the Operations and Safety Committees. A member suggested process improvement that would require all committees involved to sign off on the proposal before a proposal is released for public

comment. This may slow the policy development process down further, but will allow for broader support going in to public comment.

## 2. Review of Committee Goals

The Committee reviewed its 2009-2010 initiatives, and what had been done to meet these goals to date:

- Evaluate current status of screening and diagnostic testing for donor disease transmission, and recommend appropriate evidence-based OPTN policy concerning donor testing and screening for transmissible disease.
  - HTLV screening for potential donors eliminated in November 2009; and
  - Policy 2.0 and 4.0 rewrite currently out for public consideration.
- Develop community awareness materials relating to disease transmission concepts.
  - H1N1 guidance for the transplant community;
  - First DTAC newsletter released February 2010; and
  - Malignancy Subcommittee's manuscript is nearing publication.
- Collaborate with the Centers for Disease Control (CDC) to review current definition of high risk donors and incorporate new definition of high risk donors through appropriate evidenced-based OPTN policy.
  - CDC is working independently on this project with an expert panel that includes several DTAC members; and
  - Once the document is complete, some policy modifications will be needed to bring policy in line with the new definition, including updating the reference to the document that appears as a footnote in current policy.

## 3. Living Donor Screening Subcommittee

The Committee was provided an update on the Living Donor Screening Subcommittee's work to review the Living Donor Committee's current guidance document regarding infectious disease and cancer screening for potential living donors and provide feedback for future policy development. The Subcommittee met by teleconference on March 17 (**Exhibit A**) to discuss infectious disease screening and again on April 8, 2010 (**Exhibit B**) to discuss cancer screening in order to develop its recommendations to the Living Donor Committee.

Without additional discussion, the following list of tests currently required for potential deceased donors and recommended for potential living donors was recommended as a requirement for all potential living donors and for inclusion in policy language:

- CMV (Cytomegalovirus);
- HIV 1,2 (Human Immunodeficiency Virus);
- HBsAg (Hepatitis B surface antigen);
- HBcAB (Hepatitis B core antibody);
- HBSAB (Hepatitis B surface antibody);
- HCV (Hepatitis C Virus antibody and NAT); and
- RPR (Rapid Plasma Reagin Test for syphilis).

The Subcommittee also recommended the following additional screening for potential living donors:

- HTLV-1 Screening;
- Tuberculosis (TB) Screening (testing type unspecified); and
- Epstein-Barr Virus (EBV) (VCA and EBNA testing if recipient is EBV seronegative).

HTLV-1 Screening. It was noted that while Human T-cell Lymphotropic Virus (HTLV-1) antibody testing requirements are no longer in place for potential deceased donors, screening potential living

donors allows for more time to complete testing without requiring overnight STAT runs in expensive testing machinery made to run many samples at once.

After considering the HTLV-1 donor screening issue in June 2009, the Board of Director's motion specifically removed the testing requirement from **deceased** donors. If a positive screening result came back for a potential living donor, there would be ample time to run consequent confirmatory testing to rule out any false positive screening results. This would not be the case for deceased donors, and the high false positive rate in addition to the expense related to running single STAT screening samples on a high throughput testing system.

The need for education was noted as a concern here, as confusion may arise within the community regarding why HTLV-1 is not required for deceased donors but is considered to be of importance for a potential living donor. Expense was also raised as an issue for consideration. It was suggested that the incidence of disease in the U.S. is very low and this may be a donor screening test not be covered by potential recipient insurance, bringing very little gain for a high cost.

It was pointed out that the principle of "do no harm" should be critically considered here. With this principle as a focus, most would agree that going a step above and beyond deceased donor screening is appropriate to protect potential recipients from donor-associated risk. The additional time available for living donor evaluation as opposed to deceased donor evaluation allows for additional testing. HTLV-1 screening information may be important to select the most appropriate donor for a recipient that will include the least risk. HTLV-1 screening is still completed for blood products and this screening is readily available on a daily basis, making cost less of an issue than testing deceased donors on a STAT basis as needed. True risk to a recipient of a HTLV-1 positive donor organ is low, but not zero.

Based on the distinction made by the Board of Directors that this screening requirement should be eliminated for deceased donors, and that the fact that living donor screening allows for time to run testing in batched format and confirmatory testing as needed and prevent potential transmission of disease from living donor to recipient (that has been proven as transmissible outside of the United States), the Subcommittee agreed that this was a reasonable requirement based on data<sup>1</sup> such as it exists.

Geographic origin of the donor may make HTLV-1 an issue for concern. The Committee agreed that if this issue is highly contentious, another option would be to consider screening completed on a case-by-case basis based upon the a potential living donor's history of potential exposure in an endemic area-including where he/she is from or where he/she has traveled (endemic areas). The point was made that this may be challenging since HTLV may be spread through certain types of contact with individuals from endemic areas.

In the field of transplantation, the community must be willing to accept a balance- where the number of transmissions is acceptable in order to balance the known false positives and discards in order to be stewards of a limited resource, donor organs. What is "safe enough" for the transplant candidate population? Organ transplant cannot be held to the same requirements as blood and tissue due to testing time constraints and the shortage of donor organs versus need for transplant.

It was also suggested that if the tissue community discontinues HTLV-1 screening, then the OPTN may want to consider following suit since this screening is not currently required for deceased donors due to time constraints, high false positive results and low incidence of disease.

HCV NAT Screening. While considering HCV testing types, Members discussed whether to require antibody and nucleic acid testing (NAT) in all instances due to the longer window period (time to detection of infection by a specific testing method) involved with antibody testing; further there are

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<sup>1</sup> Kaul DR, Taranto S, Alexander C et al. Donor Screening for Human T-cell Lymphotropic Virus 1/2: Changing Paradigms for Changing Testing Capacity. **American Journal of Transplantation.** 2010; 10 207-213.

numerous reports of sero-negative infected individual in the US. Living donor evaluation was again acknowledged as allowing more time for screening than that for deceased donors. As a result, both HCV antibody testing and NAT would be an appropriate and reasonable requirement for screening.

The Subcommittee suggested that the following screening tests not be required in required:

- Toxoplasma- do not require for potential living donors, only relevant in heart donation and not applicable for live donors;
- Strongyloides- completed on a case-by-case basis based upon the a potential living donor's history of potential exposure- including where he/she is from or where he/she has traveled; and
- Trypanosoma cruzi (T. cruzi) - completed on a case-by-case basis based upon the potential living donor's history of potential exposure- including where he/she is from or where he/she has traveled.

It was noted that a Donor Derived Disease Consensus Conference will be held prior to the 2010 American Transplant Congress (ATC) on May 1, 2010. Discussion at this conference will focus specifically on TB and West Nile Virus (WNV). The Subcommittee will wait for feedback from the consensus conference before finalizing a recommendation on specific screening recommendations for these two diseases.

Cancer Screening. For potential living donor cancer screening, Subcommittee members agreed that general, age appropriate screening guided by the American Cancer Society (ACS) Guidelines is appropriate for potential living donors:

[http://www.cancer.org/docroot/ped/content/ped\\_2\\_3x\\_acs\\_cancer\\_detection\\_guidelines\\_36.asp](http://www.cancer.org/docroot/ped/content/ped_2_3x_acs_cancer_detection_guidelines_36.asp).

The Subcommittee agreed with the current recommendations put forth in the current liver and kidney guidance documents, including breast, cervical, colon, prostate and skin cancers, and also plans to reference the Malignancy Subcommittee's upcoming publication regarding the categorization of donor tumor transmission risk as an additional resource.

During the Subcommittee's April 8, 2010, discussion of appropriate screening/guidelines for living donors regarding cancer, a question arose regarding any living donors developing post-donation malignancies. UNOS Research staff presented findings related to this question at the full Committee meeting (**Exhibit C**).

Living donor follow-up is currently limited to two years post-donation without any questions specific to malignancies. Staff examined living donor deaths since 10/25/1999. A total of 61,770 living donor recoveries were completed between 10/25/1999 and 3/31/2009.

- The cause of death for donors found in Social Security Death Master File (SSDMF) and not OPTN data was obtained through calls to the transplant center.
- Most causes of death were unknown, but 25 cases identified as due to cancer (24 kidney and one liver).
- Median time from donation to death was 3.3 years with minimum of 6 months.
- Most were in 35-64 y/o age range.
- One was >65 y/o
- Eighteen of the 25 cases were reported as unknown cancer, 4 were reported as lung cancer, 1 bone, 1 brain, and 1 pancreas cancer was reported.

The Committee was interested in following up on the recipients of these living donors to determine recipient and graft survival as well as whether any of these patients also developed cancer.

After summary and discussion of the Subcommittee's recommendations, the Committee voted in favor of presenting this feedback formally to the Living Donor Committee. (*12 in favor, 1 opposed, 0 abstentions*).

Staff noted that HRSA has asked that the OPTN develop more specificity in its living donor requirements in the area of living donor evaluation and informed consent. Historically, there has been great pushback from the professional societies on this area. External stakeholders, including executive leadership from the American Society of Transplantation (AST), American Society of Transplant Surgeons (ASTS), and North American Transplant Coordinators Organization (NATCO), met with HRSA and UNOS representatives to develop a new process for getting clinical input into OPTN policy development that involves provisions for medical care. The specific make up of this new review group is still being finalized. As a result, this Committee's screening recommendations for potential living donors will probably be reviewed by this newly formed group and not be acted upon directly by the Living Donor Committee until feedback is received. It was suggested that this external group should include transplant infectious disease representation, but staff noted this would be dependent on what types of representatives the professional organizations chose to select for participation and/or representation.

#### 4. Review of Potential Disease Transmission Events

The Committee completed its semi-annual review of potential disease transmission events reported to the Patient Safety System<sup>®</sup>. Eighty cases were reviewed and classified based upon the probability of donor-derived transmission.

- Members to remove the expected/unexpected category for future case consideration.
- Members suggested that cases be grouped into categories to better focus on process improvements and determine which categories (or even specific cases) should be considered by the Operations and Safety Committee. Examples of these process categories included: communication, repeat testing, and false positive or negative test results.
- After discussion on how to best categorize a number of cases, members agreed upon the creation of a new classification, "Unlikely." This classification will be defined as "inadequate testing to definitively exclude transmission and no documented disease, but clinical circumstances make diagnosis unlikely."

#### 5. Malignancy Subcommittee Update

The Committee received an update on the Malignancy Subcommittee's draft manuscript that is meant to provide guidance to the transplant community by categorizing relative tumor-independent transmission risk when considering a donor (**Exhibit D**). The Subcommittee populated risk categories with individual tumors according to the best data available, using a three-pronged approach to:

- Define an overall framework to categorize relative transmission risk (tumor independent);
- Populate risk categories with individual tumors according to best available data; and
- Address special emphasis topics based on cases frequently seen or highly discussed within the Committee, including renal tumors and central nervous system tumors.

The tumor transmission risk categories developed for the manuscript appear below in Table 1. The Subcommittee's method for development was similar to the European approach for classifying risk of malignancy transmission. It is based on a log rather than a linear scale, and is considered by the Subcommittee to be quite conservative. The Subcommittee considered anything over 1% a significant risk of transmission, but was careful not to prohibit use. Instead, it favored exercising clinical judgment based upon a potential candidate's situation.

Risk Category		Definition		Recommended Clinical Use (with informed consent)
		Nominal	Frequency estimate	
0	No significant risk	No active malignant tumor or history of tumor	0%	Standard
1	Minimal	Literature suggests minimal risk	0-0.1%	Use based on clinical judgment
2	Low	Literature suggests low grade risk	0.1-1%	Use in recipients at significant risk without transplant
3	Indeterminate	Literature suggests significant risk	1-10%	Not recommended: on occasion, lifesaving transplant may be acceptable
4	High	Literature suggests high risk	>10%	Discouraged except in rare and extreme circumstances
U	Unknown	Evaluation incomplete or no literature	N/A	Use based on clinical judgment

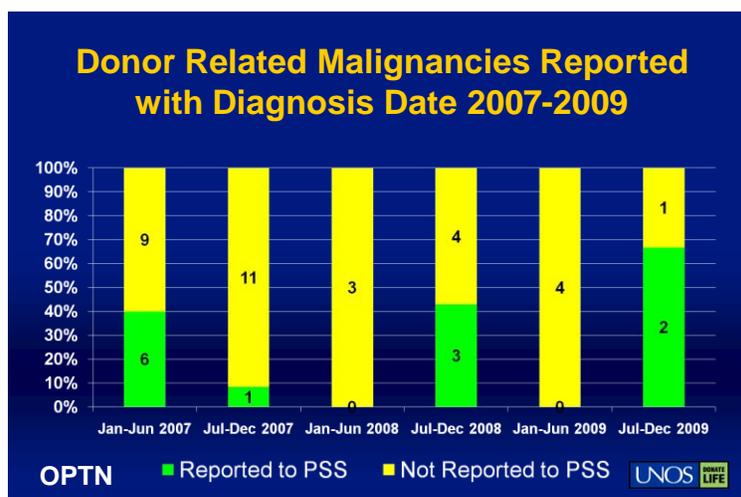
**Table 1:** Tumor transmission risk categories

A question was raised regarding whether the manuscript would include advice on how to handle renal cell carcinomas- specifically if kidney transplant should be pursued if a tumor was found in one kidney and not the other. This is not addressed in the paper. It was also recommended that an editorial be developed to explain the thresholds outlined in this paper, and why the authors agreed or separated from the European perspective, and why. A final review of current literature will be completed before finalizing the draft manuscript to journals for publishing consideration.

After the presentation, the Committee voted unanimously to update the Board of Directors regarding this manuscript and pursue publication in a transplant journal (*13 in favor, 0 opposed, 0 abstentions*).

Donor-Related Malignancies Reported on Follow-Up Forms but NOT to the Patient Safety System® (PSS). UNOS Research Staff presented data the Committee requested during its September 9, 2009, meeting regarding donor-related malignancies not reported to the PSS (**Exhibit E**). Recipient follow-up forms reporting post-transplant malignancies as “donor-related” and diagnoses from 2007-2009 were matched up with cases reported to the PSS and reviewed by the Committee.

Forty-four cases were reported on Post-Transplant Malignancy forms during this time period, but only 12 of those (27.3%) were also reported to the PSS, as depicted below in Figure 1. The median time to diagnosis of those reported to the PSS was 208 days as compared to 1171 days (3.2 years) for those reported only on the post transplant malignancy forms.



**Figure 1:** Donor Related Malignancies Reported with Diagnosis Date 2007-2009

There does not seem to be any clear pattern of improvement in the reporting of these cases to the PSS over time. Staff is completing follow-up calls to those centers who did not report to the PSS, which was implemented in March 2006. Two of the cases reported on post-transplant malignancy forms as donor-related were done so at 17 years post-transplant. There is nothing in the donor chart that indicated donor malignancy. While additional calls are still being completed, one case is believed to be donor-related, and a request was made to make this report to the PSS for Committee review. The center noted that it was unaware of OPTN malignancy reporting requirements for the PSS, as their transplant infectious disease team handles reporting for all infectious disease cases. Staff will continue to follow up on other outstanding cases and update the Committee during its monthly calls.

The UNet<sup>SM</sup> help documentation related to this form does not include any reference to reporting potential donor related malignancies to the PSS. The Committee recognized the need for additional education in this area, including updates to UNet<sup>SM</sup> help language and perhaps an article in the newsletter to remind members that the current reporting requirements pertain to both infectious disease and malignancy. It was noted that some transplant centers appear to have reservations with data sharing, and perhaps do not take these potential transmission reviews seriously. A suggestion was made to address these concerns to the Transplant Administrators Committee and work with this group to educate transplant programs.

Additional and updated data on those cases reported as donor related post-transplant malignancies and not reported to the PSS was requested for future meetings, including:

- Continued efforts to contact transplant centers to validate the information provided on donor related tumors reported on the follow-up forms but not included in the PSS, and updates of the results of this validation; and
- Data on the number of recipient deaths related to these donor related malignancies.

Incidence of Post-Transplant Malignancies in Pediatric Recipients and Outcomes Using Donors with a History of Cancer. UNOS Research Staff presented updated data (**Exhibit F**) requested during the Committee's September 9, 2009 meeting, including:

- An update on the incidence of "adult" tumors reported in pediatric recipients, including:
  - Pre-transplant Hepatitis C virus (HCV) status in liver recipients with post-transplant liver tumors; and
  - Stratification of results by donor age group and time to diagnosis.
- The incidence of Post-Transplant Lymphoproliferative Disease (PTLD) in both adult and pediatric recipients, including
  - Stratification of PTLT results by induction.
- Outcomes of recipients of organs from donors with or without a history of cancer, including
  - Recipient malignancy history;
  - Donor's cancer free interval; and
  - Recipient age group.
- Information on the utilization of potential donors with or a history of current central nervous system (CNS) tumors, including
  - Incidence of post-transplant malignancies in recipients of organs from donors with CNS tumors known at procurement.

Of the 13,779 pediatric transplants performed from 1999-2008, 511 (4.1%) developed a post-transplant malignancy. The majority of these (434) developed PTLT. Forty-seven recipients developed recurrent tumors, and 43 of these 47 were liver recipients.

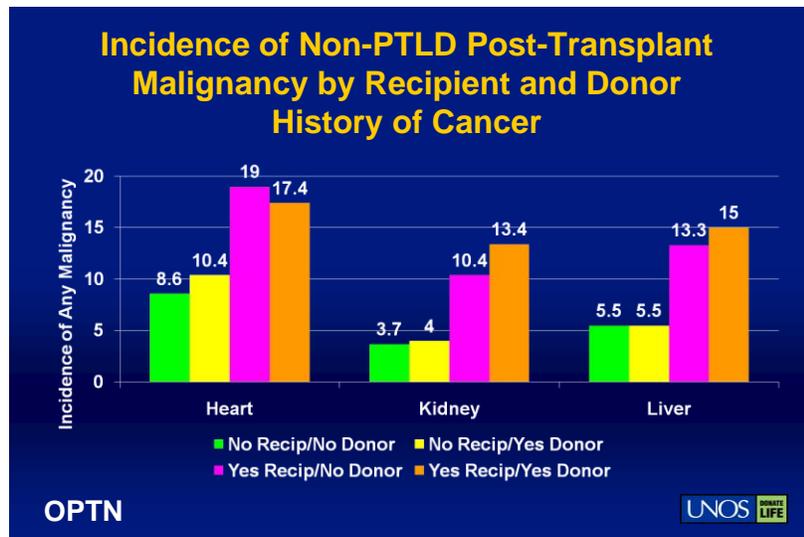
A total of 48 (0.4%) of the recipients reported a post-transplant de novo tumor. Tumor types included liver, lung, ovarian, renal, and colorectal.

- It was noted that two-thirds (32) of these recipients received organs from pediatric donors.

- Only three received organs from 35-49 year-old donors (none were older). These three cases resulted in colorectal cancer, renal cancer and sarcoma).
- Thirteen recipients received organs from donors aged 18-34. Associated cancers reported included: brain, leukemia, liver, lung, ovarian, pancreas, skin and stomach.

Staff noted that 21 of the 48 malignancies described were reported more than two years post-transplant. Eleven of the 48 were reported within 6 months of transplant, including Kaposi's sarcoma (visceral), leukemia, liver, small intestine and stomach cancer.

Next, staff updated the Committee on an analysis of outcomes by donor history of cancer. The updated data set, including all deceased donor transplants performed from 1999-2008, indicated that less than 4% of transplants (all organs combined) were completed in recipients with a previous history of cancer. There were only 232 cases where a recipient with a history of malignancy received an organ from a donor with a history of cancer. It was noted that recipients with a history of malignancy are more likely to have post-transplant malignancy, regardless of donor history, as shown graphically below in Figure 2.



**Figure 2:** Incidence of non-PTLD post-transplant malignancy by recipient and donor history of cancer

The Committee also reviewed the incidence of malignancy by cancer-free interval and patient survival rates for recipients with a donor history on cancer (excluding those with post-transplant PTLT). It was noted that none of the results were statistically significant.

Finally, the Committee reviewed data on recipient outcomes by donor cause of death, reviewing an analysis of all deceased donor transplants performed from 1999-2008. Less than 1% of all deceased donor transplants involved a donor with cause of death listed as CNS tumor. The number has decreased overall over the past few years, with just 40 reported in 2009. A review of available data indicated that recipients of these organs did have a higher incidence of reported post-transplant non-PTLD malignancy (6.5% versus 5.5% overall).

The Committee requested additional information regarding whether any of these 6.5% of cases actually developed CNS tumors. Staff will follow up with this after reviewing recipient cause of death.

Additional comments were made regarding a 2003 paper by Dr. Wida Cherikh<sup>2</sup> et al regarding associations with the type of induction immunosuppression in relation to PTLD, graft survival and patient survival after kidney transplant. The paper was provided with meeting materials as a related informational item. It was suggested that it may be time to update this paper and look at trends in other organs based upon recent experience.

## 6. Review of Policies and Bylaws Issued for Public Comment

The Committee reviewed the Policy Oversight Committee's public comment proposal, released on March 5, 2010, during its April 8, 2010 LiveMeeting®.

1. Proposed Modifications to Data Elements on the following Tiedi® forms: Transplant Candidate Registration (TCR), Transplant Recipient Registration (TRR), Transplant Recipient Follow-up (TRF), Living Donor Registration (LDR), Living Donor Follow-up (LDF), Deceased Donor Registration (DDR), Histocompatibility Form (HF), and approval of a new Explant Pathology Form for Liver Recipients. *Policy Oversight Committee*

- The Committee reviewed proposed data collection changes specifically related to its work. All members were encouraged to review the full proposal and provide individual comments as well. The Committee planned to review and respond to any public comment feedback regarding the fields it recommended during its April 14 meeting in Chicago.

After discussion, the Committee voted to support the proposed modifications (*10 in favor, 0 opposed, 0 abstentions*), but requests that the OMB consider the comments offered below:

- Deceased Donor Registration (DDR) Form Discussion

A member noted that Chagas is not a virus and should be removed from the viral detection heading.

Concern was raised that HTLV remains on the form, though this testing is no longer required by policy. Staff pointed out that NAT, Chagas or West Nile Virus tests are also optional, but that this Committee voted to propose these fields be added to provide a place to enter this data for consideration if testing is completed; collection of this information is felt to be important to guide future policy recommendations and is not available elsewhere. Help documentation can be modified to note that this is supplementary information. While the fields must be completed (using not done if necessary), the testing itself is not required.

Bronchioalveolar Lavage (BAL) specimen results were also discussed. In developing recommended additions to the data collection forms, the Chair approached the Thoracic Organ Transplantation Committee for feedback in spring 2009. The Thoracic Committee's Lung Subcommittee noted that the OPOs do not generally collect this information (since BALs are typically performed at the accepting center and not as part of the procurement), and that the DDR would not be an appropriate place to collect such information. This BAL is generally performed by the transplant center after the lung is transplanted. Ongoing discussion will take place with the Thoracic Committee regarding collecting information related to BAL.

- Transplant Candidate Registration (TCR) Form Additions Discussion

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<sup>2</sup> Cherikh, WS, Kauffman HM, McBride MA, et al. Association of the Type of Induction Immunosuppression with Posttransplant Lymphoproliferative Disorder, Graft Survival, and Patient Survival after Primary Kidney Transplantation. **Transplantation**. 2003; 76(9) 1289-1293.

Concern was noted regarding the addition of a single HIV, HBV surface antigen, and HCV serologies on the TCR. It was pointed out that the SRTR requested these additions at time of listing to use for risk adjustment and the center specific outcomes reports. A member questioned whether serology results alone would be adequate for this use. Members agreed that HCV serology alone will provide incomplete data that may affect risk assessment stratification. If this data is to be used for risk adjustment, the Committee favors also including confirmatory NAT for candidates with positive serology results and potentially to confirm in seronegative patients with high risk of HCV.

A suggestion was offered to change the title heading from “serology” to “viral detection” with help documentation asking the user to provide confirmatory NAT results when available.

- Transplant Recipient Registration (TRR) Form Additions Discussion

No additional comments from the Committee the TRR proposal. During the discussion of viral detection fields on the TCR, it was noted that it would be appropriate on the TRR to capture NAT confirmatory results in the case of positive HCV serology results.

- Transplant Recipient Follow-up (TRF) Form Additions Discussion

There was agreement that requesting post-transplant serology results sequentially for the first five years post-transplant is unnecessary and overly burdensome. The quality of the data was also questioned, suggesting that the person completing the form may not go back to pull this information accurately. Sequential testing is appropriate for recipients of organs from donors at increased risk for blood-borne pathogens. Otherwise, this information should only be necessary at six months or one year post-transplant as related to potential disease transmission. All agreed that this complements with the recommendations from the NAT Consensus Conference regarding follow-up of recipients of high risk donors which recommends post-transplant screening by serology and NAT at months 1, 3, and 12 post-transplant.<sup>3</sup> It was noted that the Committee’s intention, when making this recommendation, was not for five years of follow-up and collection of results through one year would be adequate.

It was also noted that in the case of donor transmitted malignancy, most cancers would manifest within a year, and not require five years of post-transplant follow-up

Staff stated that the current form is used for five years. Changing forms to allow for these questions only at six months or one year may incur additional programming costs. Staff will look into this further and this suggestion will be forwarded to the POC.

- Living Donor Registration (LDR) Modifications Discussion

No additional comments.

The Committee reviewed feedback received thus far from other Committees, regions and individuals related to proposed fields that were recommended, modified, or deleted by this Committee during it April 14, 2010, face-to-face meeting.

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<sup>3</sup> Humar A, Morris M, Blumberg E, et al. Nucleic Acid Testing (NAT) of Organ Donors: Is the “Best” the Right Test? A Consensus Conference Report. **American Journal of Transplantation**. 2010; 10 889-899.

Thoracic Organ Transplantation Committee Feedback. The Committee discussed the frequency in which centers submit the follow-up forms, as well as mandating testing for transmissible diseases. Staff stated that centers complete a follow-up form each year. However, if a center does not perform this follow-up, it may opt to respond “not done.” The Committee discussed a potential policy addition that states that centers must test recipients of high-risk donors at 3, 6, and 12-month intervals.

The Thoracic Organ Transplantation Committee requested that this Committee comment on the proposed data elements for addition. Specifically, the Thoracic Committee wanted to consider the DTAC’s opinion on the time frame for collecting the proposed data elements. Does DTAC wish to mandate the collection of these data elements? Will the deceased donor’s classification of “high-risk” have an impact on the collection of these data elements?

*The Committee appreciates this feedback. Proposed modifications to Policy 2.0 and 4.0 language in the Committee’s March 19 public comment document require that transplant centers offer additional testing, monitoring and/or therapy as appropriate for recipients of high risk organs. The Committee realizes that it cannot recommend requiring such testing be completed as recipients must have the right to refuse this care. The current paper on NAT<sup>4</sup> recommends high risk organ recipient post-transplant screening at 1, 3 and 12 months. It was suggested that the follow-up testing interval should be directed at what will help patients, and not be based upon convenience issues related to completing OPTN forms.*

*The Committee recognizes the burden of data entry involved in recording this information. Testing will not be required but recipient centers must enter “not done” to complete the form and meet compliance requirements. Committee members talked about forms defaulting to “not done” if a positive or negative value is not entered, but was not fully comfortable with this approach either, as data coordinators may miss a field that was actually completed and not be prompted to recheck it if it defaults.*

Individual Feedback. We disagree with the question related to donor HIV status, as knowingly transplanting an organ from an HIV positive donor of any type is a violation of Federal law.

*The Committee believes that if this data is not collected, there is no way of knowing if the Federal law is being violated.*

The DDR is already a comprehensive document. By adding additional fields it becomes more cumbersome than is necessary. We specifically oppose the following additions:

- Clinical infection confirmed (positive cultures are already entered—no need to change);

*The Committee hopes this modification will decrease the data burden by no longer requiring that every positive culture is entered on the DDR, but rather only those that are clinically meaningful.*

- Type of intracranial and extracranial cancer at time of procurement may be unknown

*A child (subsequent) question will ask for site of cancer if cancer is indicated as present, and there will be an “unknown” field that can be used prior to recovery. If additional information is received prior to the 30 day form completion date, this could be updated by the OPO. OPO representatives on the Committee did note that very little updating of this form occurs within the 30 day period, and that autopsy results may be received much later. This would result in a high number of “unknown” responses, creating meaningless data. Staff noted that the form may be updated, but this would be an additional burden on OPO staff. A recommendation was made to collect this information for 6 months to 1 year to determine the rate of “unknowns” submitted. If meaningful data is not collected, the question could then be removed. The Committee believes*

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<sup>4</sup> Humar A, Morris M, Blumberg E, et al. Nucleic Acid Testing (NAT) of Organ Donors: Is the “Best” the Right Test? A Consensus Conference Report. **American Journal of Transplantation**. 2010; 10 889-899.

*that collecting this information is important to determine the denominator and the number of recognized transmissions of cancer.*

- NAT results for Chagas and West Nile Virus are not routinely done by our lab. HTLV is not a reliable test and several OPOs and tissue banks are getting away from the testing.

*These tests are not required, but are recommended for areas/seasons where these diseases are prevalent. OPOs can respond “not done.” The Committee believes, however, that collecting this data helps the transplant community better understand the denominator of donors affected and may provide insight when determining policy related to these assay. This is important not only for disease transmission, but also for organ wastage.*

- We would also like to see more fields migrate from DonorNet<sup>®</sup> to Tiedi<sup>®</sup>.

*Staff noted that any data fields added to DonorNet<sup>®</sup> that also appear on Tiedi<sup>®</sup> will have programming to cascade this information over to the Tiedi<sup>®</sup> forms to decrease data entry burden on OPO staff.*

This is in regards to the proposed modifications to the DDR form.

- The additional serologies and NAT results being added are recognized as important for capturing and data collection, but should have a default value of “not done” in order to prevent data errors.

*Staff noted that there will be a “not done” option that the data coordinator may select. There are not currently plans for the system to default to this field.*

- The type of cancer questions proposed (skin/intracranial/extracranial) should be proposed as child (subsequent) questions to the existing DDR questions regarding cancer at the time of procurement if cancer is indicated as present. If each of the current questions is answered yes, then the child questions would be the new proposed data element.

*Staff noted that type of skin cancer will be a child question to the existing question. If cancer is answered “yes,” questions regarding location will follow.*

XXXX (responding member identifier redacted) reviewed the proposed recommendations for additional data on KI/KP/PAK recipients. The addition of new data elements is redundant/irrelevant to the standard of care and will add unnecessary additional burdens on the transplant team, while further complicating the data collection process:

- CMV total is an obsolete term and not done in our institution. We do CMV IgG and CMV IgM.

*The Committee appreciates the comment and agrees that capturing only CMV IgG is appropriate on the TRR form. This data is used for mismatch outcome, and is still an important item to collect. Staff will follow up to make sure that this field is not involved in center specific outcomes reports.*

- The recommendation of routine serology testing post-transplant is not relevant and serves no useful purpose, unless triggered by a clinical event. Most recipients do their follow-up care with their own providers, returning to the transplant center when there is a problem. They do not do routine serology unless there is an indication for it. Please remember that adding additional data elements makes getting information from the primary care givers even more difficult. From the data coordinator perspective, providing the new data will be difficult in all cases, and impossible in many. Further, it is a non-reimbursable expense.

*Committee members urge transplant centers not to wait for clinical signs or symptoms of infection- that is too late. Early intervention will benefit the recipient. This is especially critical for recipients of high risk donor organs. It was noted that ethically, if you are informing a patient that they are accepting an organ that may pose a risk of infection, you have an obligation to confirm that no disease has been transmitted. Disease transmission should be considered before disease actually manifests itself. Follow-up testing would be covered during the global period immediately after transplant, usually 30-90 days post transplant, and in almost all cases that transplant center is still seeing recipients at one month post transplant.*

Cancer questions should be “child questions” of existing cancer questions (e.g. “type of skin cancer” should not be required unless skin cancer question is answered affirmatively).

*The Committee appreciates the comment and confirms that this is, in fact, how the question will be set up on the form.*

Additional comments related to DTAC recommendations that are received by Friday, April 16, will be reviewed at a later date. The Committee will review all fields that it added successfully to the forms on an annual basis to reassess the need for data elements, and eliminate items in the future that are not useful.

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The Committee also reviewed the ten proposals released for public comment on March 19, 2010, during its April 14, 2010, meeting in Chicago.

1. Proposed Ohio Alternative Local Unit (ALU) *Liver and Intestinal Organ Transplantation Committee*
  - Upon review, the Committee determined that it had no comment regarding this issue.
2. Proposed OneLegacy Split Liver Alternative Allocation System *Liver and Intestinal Organ Transplantation Committee*
  - Upon review, the Committee determined that it had no comment regarding this issue.
3. Proposed Region 2 Split Liver Alternative Allocation System *Liver and Intestinal Organ Transplantation Committee*
  - Upon review, the Committee determined that it had no comment regarding this issue.
4. Proposal to Develop and Efficient, Uniform National Pancreas Allocation System *Pancreas Allocation Committee*
  - Upon review, the Committee determined that it had no comment regarding this issue.
5. Proposal to Modify OPO and Transplant Center Requirements for Screening, Communicating and Reporting All Potential or Confirmed Donor-Related Disease and Malignancy Transmission Events *Ad Hoc Disease Transmission Advisory Committee*

- The Committee sponsored this proposal, and will review all individual, committee, and regional responses it receives.
6. Proposal to Update HLA Equivalences Tables *Histocompatibility Committee*
    - Upon review, the Committee determined that it had no comment regarding this issue.
  7. Proposal to Require that Deceased Donor HLA Typing be Performed by DNA Methods and Identify Additional Antigens for Kidney, Kidney-Pancreas, Pancreas, and Pancreas Islet Offers *Histocompatibility Committee*
    - Upon review, the Committee determined that it had no comment regarding this issue.
  8. Proposal for Placement of Non-Directed Living Donor Kidneys *Living Donor Committee*
    - Upon review, the Committee determined that it had no comment regarding this issue.
  9. Proposal to Require Reporting of Non-Utilized and Redirected Living Donor Organs *Living Donor Committee*
    - Upon review, the Committee determined that it had no comment regarding this issue.
  10. Proposal to Require Use of a Standardized, Internal Label that is Distributed by the OPTN and that Transplant Centers Notify the Recovering OPO when they Repackage an Organ *Organ Procurement Organization (OPO) Committee*
    - The Committee voted unanimously in favor of the concept outlined by the OPO Committee (*13 in favor, 0 opposed, 0 abstentions*), but requested that the OPO Committee consider concerns related to the actual labeling system it proposed, including:
      - No double verification stage built in for 2<sup>nd</sup> person to review and confirm what was entered on the label;
      - A recommendation to affix the vessel label to the jar rather than tying to the jar or affixing to the outer bag in which that the vessel jar is transported;
      - Only one donor identifier currently appears on the pilot test label (the UNOS Donor ID);
      - A recommendation that current technology like bar coding be considered to avoid the potential for human error in entering information; and
      - Colors currently used for pilot program labels are somewhat close and could be easily confused. Please consider reassigning colors, or using colors that are not so close in nature to avoid labeling errors.

It was also noted that the packaging and labeling process is already very onerous. She suggested that a bar coding system be implemented nationwide to streamline the process and reduce the opportunity for human error in filling information in on labels by hand. This issue is also being considered by the Health and Human Services' Advisory Committee on Blood Safety and Availability (HHS ACBSA). There was agreement that practice for organ package labeling should be aligned

with tissue if at all possible for the sake of consistency. It was anecdotally noted that a large number of patient safety situations arise from packaging and labeling errors, but that, to date, a root cause analysis has not been completed to identify specific categories of these incidents.

7. Newsletter Update

Statistics were shared regarding hits to the new UNOS Communications e-newsletter/blog, which includes the Committee's first electronic newsletter, (**Exhibit G**). To date, the DTAC newsletter has received more hits than any other page on the blog. Committee members and staff commented on the positive feedback that was received regarding this effort. The Committee plans to release two newsletters per year and future articles on Coccidioidomycosis and cancer/malignancy reporting were recommended. New members for this group will be needed as the Committee membership rotates at the end of June.

8. Operations and Safety Committee Update

The Committee received an update from the Operations and Safety Committee Chair on this group's new focus and charge since the Operations Committee was renamed (**Exhibit H**). This Committee hopes to take what it has learned from observing this Committee to develop its own case review and categorization plan and share general patient safety information with members through an electronic newsletter. This Operations and Safety Committee will look at policy and/or process gaps and education opportunities for the community.

An overview of work being done to address vessel monitoring and safety and the development of a related policy modification anticipated for public comment in fall 2010 were also discussed. The Committees hope to eliminate the risk of Hepatitis B and C transmission through the use of donor vessels in secondary recipients.

9. Discussion of Developing Public Comment Proposal from the Ad Hoc International Relations Committee

The Committee considered several questions posed by the Ad Hoc International Relations Committee (AHIRC) regarding its proposal to clarify and improve policies on importing foreign deceased donor organs (**Exhibit I**). The AHIRC is seeking feedback from several committees as it works to develop and prepare a public comment proposal that may be released for formal consideration in fall 2010. Specifically, the AHIRC asked this Committee to consider:

- Does the current draft proposed policy address concerns this committee has about the foreign import of an organ?
- What other potential disease transmission concerns should be addressed in this policy section?

Imported organs currently come to the U.S. from Canada, Bermuda, and the Bahamas (and two from Panama). Only 44 organs have been imported in the last five years. Concerns regarding whether the importing OPO can confirm that appropriate FDA-approved screening assays and the receipt of complete medical-social provided in English, and communication of potential disease transmission for either the donor or recipients (it was noted that typically these organs are not handled by the local OPO and details are considered by the accepting transplant center). As written, the policy encourages repeat serology tests; though this may not be necessary if an FDA-approved assay was used for testing at the foreign site. To date, there have been no adverse events reported involving imported organs. No potential disease transmissions have been reported involving these organs, but this could be problematic if a foreign donor or recipient became ill and this information was not communicated to the U.S. recipient; there is currently no mechanism in place to coordinate communicate reporting of such transmissions.

It was recognized that donors from Bermuda and the Bahamas are contracted through U.S. OPOs and Canadian organs come from a medical system that is comparable to the U.S.; many, but not all, screening tests used in Canada are also FDA-approved. Special concern should be focused on other sources of organs, including wider areas of the world with improved packaging and transport methods. It was noted that current policy does not specify between countries of origin, so minimum standards may be more appropriate for consideration. It was also noted that the current draft appears to encourage accepting import OPOs to repeat serologies, even if original testing is FDA-approved. Members agreed that language should be modified to state that testing should only be repeated when non FDA-approved screening tests have been performed.

Testing variation was also recognized as a potential problem, as different countries may have testing unique to a specific geographic area – i.e. Chagas testing for endemic areas. Incidence and the potential for dormancy of disease in a potential donor from a specific area are critical to acknowledge regardless of living or deceased donation. It was acknowledged that all imported organs do not go through an OPO, as some may be sent directly to a transplant center. Committee members were concerned that a decision maker at a center may not be familiar with the types of FDA-approved testing that may be warranted.

Additional concerns were raised regarding confirmation that donation of an organ(s) was not coerced and did not involve valuable consideration. The AHIRC liaison noted that in the recent import of organs from Panama, the Panamanian government had to authorize the export of the organs. Such documentation was seen by the AHIRC as a way to ensure that the agency is reputable and legitimate. It was noted that in the case of one of the Panama imports, directed donation was involved.

This information will be shared with the AHIRC and any related modifications to the draft proposal will be shared with this Committee prior to public comment release.

#### 10. Analyzing Trends and Patterns in Bacterial, Tuberculosis and Fungal Case Reporting

Committee members received a brief update on ongoing efforts to analyze trends and patterns noted in bacterial, tuberculosis, and fungal cases reported to the Patient Safety System. Work is ongoing, and the Committee plans to develop manuscripts and/or guidance documents for each of these areas in an effort to educate the transplant community and help prevent potential transmissions based upon what has been learned from cases the Committee has reviewed. Feedback from the bacterial review will be used to respond to a memo from the Membership and Professional Standards Committee (MPSC).

Bacterial Cases Sixty-one potential bacterial cases were reported during the review period, but 23 were Mycobacterium or TB-related and removed. Four of the remaining cases were syphilis and also excluded. Of the 34 remaining cases, the vast majority did not involve donor-derived infection. Of the proven cases of donor-derived infection, problems were noted with poor communication and bad choice of donor organ (acceptance). It was noted that the new Patient Safety Contact should help improve communication between OPOs and transplant centers. Education is necessary to help the community consider issues of organ selection, organ soilage, etc. It was noted that several of the organ soilage cases involving antimicrobial resistance were presented at an APO Medical Directors meeting. Donors with open abdomens ultimately led to poor recipient outcomes in multiple recipients. Members debated on what level of response necessary for cases of bacteremia and/or organ soilage in the donor. The Committee agreed that bacteremia is probably the least likely to be recognized as a donor-derived transmission. They hypothesized that transmission is high, but is frequently managed without full recognition using basic post-transplant prophylaxis. Additionally, documentation is difficult to ascertain, specifically:

- What did you know and when did you know it?
- What prophylaxis was administered for donor and recipient(s)?

It was noted as difficult to know where to document new information regarding cultures and sensitivities. An OPO member of the Committee noted that there is no date/time stamp on DonorNet<sup>®</sup> to delineate what was posted and known to the center at time of offer versus post-recovery and post-transplant. It was also noted that the electronic medical record makes it difficult for OPOs when becoming involved in potential new donor cases, and layout varies from hospital to hospital- making information difficult to find.

A manuscript will be developed using this information for educational purposes and a final response to the MPSC regarding possible development of a policy or guidance document regarding a time period to assess for previous positive cultures for donors that were admitted to the hospital prior to donor evaluation will be submitted.

Tuberculosis (TB) There has been a significant increase in the number of TB cases reported over the last two years, with probable or proven transmission in several events. There is no FDA-approved donor screening test for TB, and the OPO community currently relies on donor medical-social history. A PPD (purified protein derivative skin test) is not an option due to logistics and there is little data available on interferon-gamma release assays in deceased donors.

Areas of concern include cultures obtained as parts of routine patient care are often difficult to track down or results come back post-transplant. There is also poor communication regarding the donor specimen(s). Sharing information after the patient becomes a donor- even with local/state health department involvement is frequently problematic if they do not know that donation was pursued. Some donor hospitals discard specimens once death has been declared, without completing testing. Additionally, suspicious findings, such as nodules found at time of procurement, may not be adequately shared with recipient centers. Positive results indicating great potential for active TB may not be adequately managed by the recipient centers, which is out of this Committee's purview.

Fungal Cases Reporting of fungal cases reached its high point in 2009. Confusion was noted in reporting, and there is a need to improve screening of the donor pool. Coccidioidomycosis was seen as a definite area for improvement, as these organs will not be refused if the fungus is known, but recipients must receive treatment to do well. Rhizopus and Aspergillus cases reported to the PSS both resulted in several deaths. There were flags that were missed and could have benefitted the recipients. Submersion deaths must also be suspected for recipient safety. The critical learning point is that the OPO must identify risk factors and share this information with centers early in the organ offer process because there will be a delay in getting fungal test results.

A recommendation was made to develop a donor algorithm for evaluation and recognition of classic red flags in donors at risk for fungal infection as a learning tool. This type of information will be especially helpful for Region 5, where Coccidioidomycosis is endemic.

#### 11. Update on Follow-Up Donor Screening Survey

The Committee briefly discussed its October 2008 OPO Survey regarding donor screening and the need to do a follow-up survey based upon changing test availability and the upcoming changes to CDC "high risk" donor definitions. Information gathered as part of this survey may ultimately lead to donor screening policy changes. Plans to work with AOPO on the future effort for release in winter 2010 were discussed in order to encourage 100% participation in this effort. Additionally, plans were made to streamline the survey itself, using more multiple choice and fewer free response questions. A suggestion was made to add a question or two regarding H1N1 Guidelines.

A request for volunteers to participate in a Survey Subcommittee was announced, with interested members responding to the Chair or Committee Liaison.

12. Case Workflow – Polling the Committee on Case Classification

UNOS Patient Safety Staff reiterated the importance of polling the Committee for their expert opinion regarding probability of donor-derived nature of each case after the 45 Day Report is received. Staff announced and briefly demonstrated a new method for polling members, which will be implemented using the external SharePoint site for all 2010 cases. Polling is expected to streamline the case review process and allow for more time for discussion of other items during face-to-face meetings.

Completion of surveys and expediting the case closing process will allow staff to finalize its process for closing cases and notifying members of the outcome of the Committee's review.

13. Welcome and Introductions

The Chair welcomed Committee members to the April 14, 2010, meeting, and introduced a new UNOS staff member and Director of OPTN Board and Committee Operations, Brian Shepard, and a new CDC liaison who will be working with the Committee, Dr. Eileen Farnon.

14. Recognition of Outgoing Committee Members and New Leadership

Outgoing members with terms ending in June 2010 were recognized for their service during the April 14, 2010, meeting. The outgoing Chair was also recognized for his service and dedication to further developing the Committee and its case review process. The incoming 2010-2012 Chair and Vice Chair, Drs. Emily Blumberg and Michael Green, were also introduced.

## DTAC Attendance October 2009 – April 2010

NAME	DAY	10/1 2009	10/22 2009	11/12 2009	12/10 2009	1/14 2010	2/11 2010	2/18 2010	3/11 2010	4/8 2010	4/14 2010
	FORMAT	Call	Call	Call	Call	Call	Call	Call	Call	Call	In Person
	COMMITTEE POSITION										
Michael Ison, MD	Chair	X	X	X	X	X	X	X	X	X	X
Michael Nalesnik, MD	Vice Chair	X	X	X	X	X	X	X	X	X	X
Emily Blumberg, MD	At Large	X	X		X	X				X	X
Peter Chin-Hong, MD	At Large	X	X	X						X	X
J. Michael DiMaio, MD	At Large							X			X
Jon Gockerman, MD	At Large										
Michael Green, MD, MPH	At Large	X	X		X	X	X			X	X
Richard Hasz, Jr., MFS	At Large	X		X	X		X		X		X
Bernard Kubak, MD, PhD	At Large	X			X		X	X	X	X	X
Daniel Lebovitz, MD	At Large	X	X	X		X	X		X		X
Timothy Pruett, MD	At Large	X	X							X	X
Alison Ballew Smith, RN, BSN	At Large	X			X		X		X	X	X
Lewis Teperman, MD	At Large		X							X	X
Brahm Vasudev, MD	At Large			X	X		X			X	X
James Bowman III, MD	Ex Officio, HRSA	X				X					X (phone)
Elizabeth Ortiz-Rios, MD, MPH	Ex Officio, HRSA		X	X		X		X	X		X (phone)
Bernard Kozlovsky, MD, MS	Ex Officio, HRSA		X			X	X			X	
Matthew Kuehnert, MD	Ex Officio, CDC										
Shandie Covington, BS	Committee Liaison	X	X	X	X	X	X	X	X	X	X
Kimberly Parker	Support Staff	X	X	X	X	X	X	X		X	X
Sarah Taranto	Support Staff	X		X		X	X	X	X	X	X
Kimberly Taylor, RN	Support Staff	X	X	X		X	X	X	X	X	X
Lin McGaw, RN, MEd	Support Staff				X						X
Stacey Burson	Support Staff	X				X	X	X	X	X	X (phone)
Mary D Ellison, PhD, MHSA	Support Staff										X
Brian Shepard	Support Staff										X
Robert Metzger, MD	Support Staff						X				X
Willie Bower, MD	CDC support		X			X	X	X	X		X
Debbie Seem, RN, MPH	CDC support		X	X	X		X		X	X	
Eileen Farnon, MD, DTM&H	CDC support									X	X
Vipra Ghimire	Staff (guest)										X (phone)